Journal of Clinical and Biomedical Sciences

Editorial

Acute Aluminium Phosphide Poisoning: An Under reported Problem in India.

Harish R[1*], Rajkumar MG[2], Shashidhar K N[3]

1. Associate Professor, Department of Biochemistry, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar.
2. Assistant Professor, Department of Forensic Medicine & Toxicology, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar.
3. Professor & Head, Department of Biochemistry, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar.

One of the foremost methods of committing suicide in India is aluminium phosphide (AlP) poisoning. AlP toxicity is induced by the discharge of phosphine gas, which induces cell hypoxia and circulatory failure because of suppression of oxidative phosphorylation. There is no specific antidote for AlP toxicity and treatment is mostly supportive. Although it is a common suicidal agent, the documented numbers are small due to the lack of patients who eventually reach tertiary care, due to the extreme toxicity of AlP.

Since the 1940s, AlP has been used as a rodenticide and isolated incidences of fatal exposure to phosphine gas generated from AlP have been recorded in the literature from bulk wheat shipments utilizing AlP as an herbicide between 1967 and 1980.[1] This poisoning was unknown in India till 1980 and M G M Medical College in Indore reported the first case in 1981.[2] The poisoning has been progressively growing in frequency and it is now the most common poisoning in the country's northern and central areas.

The fatal dose of AlP is 0.15-0.5 g in a 70kg man.[3] AlP discharges a large amount of phosphine gas when ingested. AlP produces phosphine gas when it combines with air, water, or gastric acid. Phosphine is a colorless, very poisonous gas with an odor similar to garlic or decaying fish. Phosphine disrupts the oxidative phosphorylation in mitochondria leading to ATP depletion due to non-competitive inhibition of mitochondrial cytochrome oxidase of the electron transport chain.[4]

$$AlP + 3H_2O \rightarrow Al(OH)_3 + PH_3;\ AlP + 3\ H^+ \rightarrow Al_3+ + PH_3$$

As a mitochondrial toxin, phosphine prevents enzyme glycerophosphate dehydrogenase. Free radicals are created during phosphine poisoning, which exacerbates damage and leads to multi organ failure. Rapid development of shock, metabolic acidosis, cardiac arrhythmias and respiratory failure are the constellation of manifestations leading to the high fatality rate. Hemolysis can also occur as a consequence of phosphine poisoning; however, it is rare.[5] The severe toxicity of AlP particularly affects cardiac and vascular tissue which can manifest as severe and refractory hypotension, congestive heart failure, electrocardiogram abnormalities, myocarditis, pericarditis and subendocardial infarction. The frequency of hypotension ranged from 76% to 100%, which is an essential feature of AlP toxicity.[6]

The effectiveness of a gastric lavage after consumption is mainly determined by the duration of exposure to the poison and should be carried out immediately. As potassium permanganate $KMnO_4$ (1:10000) oxidizes phosphine to harmless phosphate, it is utilized for gastric lavage. It has been observed that phosphine is a hard nucleophile and the reactive oxygen species released from the resolution of $KMnO_4$ do not react with each other; as a result, there is no concrete evidence that $KMnO_4$ is effective against AlP toxicity.[7, 8]

Marashi et al observed that slurry of activated charcoal aids in the removal of phosphine from the body. Activated charcoal has a large internal surface area made up of pores (10 Å to 20 Å). It adsorbs poisons with a modest molecular weight of about 100 Da to 800 Da with ease. AlP has a molecular weight of roughly 58 Da making the involvement of activated charcoal in AlP poisoning is once again speculative.[9]

Singh Bajwa et al used a regimen containing coconut oil with sodium bicarbonate for gastric lavage.[10] Liquid Paraffin may be used to accelerate the

elimination of AlP and phosphine from the gastrointestinal tract. In vitro experiments indicate that vegetable oils and liquid paraffin block the release of phosphine from ingested AlP by virtue of the physicochemical properties of AlP and its immiscibility with fat.[11] Another mechanism proposed by Shadnia S et al is that coconut oil prevents the absorption of phosphine gas by forming a protective layer around the lining of the stomach. Coconut oil further helps dilute the stomach hydrochloric acid (HCl) and inhibits the breakdown of the phosphide in the granule. Sodium bicarbonate inhibits the release of phosphine by neutralizing the HCl which in turn reduces the catalytic reaction of phosphide with HCl.[12] It is therefore beneficial to administer medicinal liquid paraffin or coconut oil to those who have ingested AlP.

As a measure to counter the acute AlP toxicity it can be attempted to reduce the cellular toxicity of phosphine gas with antioxidants or chemicals which can replenish the antioxidants. Magnesium sulfate helps scavenge free radicals through glutathione (GSH) restoration and therefore may be effective through parenteral route to replenish the antioxidant GSH in this poisoning and has also been tested for its general membrane stabilizing effects on cardiac myocytes.

Chugh et al observed the effectiveness of magnesium sulfate in relation to the dose of AlP taken and concluded that hypomagnesemia was more common with mortality and that higher levels of magnesium after supplementation significantly reduced mortality, regardless of the dose of pesticide taken.[13] Singh also reported better outcomes in patients who presented within 4 hours and started intravenous $MgSO_4$.[14] However, Siwach et al observed that there was no significant difference in dose-dependent mortality rates in patients treated with and without $MgSO_4$ and recommended the use of stronger antiarrhythmic agents in controlling some supraventricular arrhythmias.[15] Sahoo et al reported a case of aluminium phosphide consumption by a 60 year old woman with suicidal intention and developed anteroseptal acute myocardial infarction following 48 hours of hospitalization.[16]

Oghabian Z et al observed that with the administration of Dihydroxyacetone (DHA) in the dose of 7 g in 50 mL sodium bicarbonate through gavage 2 times at one hour interval showed improvement clinically in two human cases.[17] DHA is a simple monosaccharide which has shown to restore mitochondrial cytochrome C oxidase activity in animal models using mice poisoned with inhalational phosphine.[18] Rashedinia M et al demonstrated that DHA suppressed the phosphine gas induced toxicity in the HepG2 cell line by increasing the production of ATP through glycolysis.[19] However, further studies are required to ascertain the benefit of DHA in AlP poisoning.

To conclude the unavailability of a particular antidote could be a major reason that Aluminium phosphide poisoning incorporates a high mortality rate. Only possible life-saving measures in the event of poisoning with an unexposed form of AlP are supportive. Optimizing supportive care helps achieve high survival rate despite hemodynamic effects at presentation. In treatment, the primary goal is to provide effective oxygenation, ventilation and circulation until phosphine is removed.

In severe AlP poisoning continuous invasive hemodynamic monitoring is needed with early resuscitation using fluids and vasoactive agents. Extracorporeal membrane oxygenation (ECMO) combined with continuous renal replacement therapy (CRRT) also may be lifesaving. Specific treatment for AlP toxicity includes decreasing phosphine absorption, decreasing cellular toxicity and increasing renal and pulmonary excretion. Though the mechanism is unclear Dihydroxyacetone (DHA) may be an emerging antidote from bench to bedside for AlP poisoning.

References

1. Wilson R, Lovejoy FH, Jaeger RJ, Landrigan PL. Acute phosphine poisoning aboard a grain freighter: epidemiologic, clinical, and pathological findings. JAMA 1980;244(2):148-50.
2. Kabra SG, Narayanan R. Aluminium phosphide: worse than Bhopal. The Lancet 1988;1 (8598):1333.
3. Ranga GS, Dwivedi S, Agarwal M, Kumar D. Aluminium phosphide poisoning in a young adult: a suicidal cardiotoxin simulating myocardial ischaemia. J Ind Acad Clin Med 2004; 5(4):369.
4. Berry A, Singh G, Kaur S, Bala K. Aluminium phosphide: toxicity mechanism and credible treatments. World J Pharm Pharmaceutical Sci 2015;4:2277-93.
5. Hosseini SF, Forouzesh M, Maleknia M, Valiyari S, Maniati M, Samimi A. The molecular mechanism of aluminum phosphide poisoning in cardiovascular disease: Pathophysiology and diagnostic approach. Cardiovasc Toxicol 2020; 20(5):454-61.

6. Gurjar M, Baronia AK, Azim A, Sharma K. Managing aluminum phosphide poisonings. J Emerg Trauma Shock 2011; 4(3):378-84. doi: 10.4103/0974-2700.83868. PMID: 21887030; PMCID: PMC3162709.
7. Hassan S. Gastric Ventilation Along With Gastric Lavage in Celphos Poisoning: A Prospective Study. IAR J Med Scie 2021 ;2(1).
8. Senthilkumaran S, Ananth C, Menezes RG, Thirumalaikolundusubramanian P. Aluminium phosphide poisoning: Need for revised treatment guidelines. Indian J Anaesth 2015; 59(12):831-2. doi: 10.4103/0019-5049.171624. PMID: 26903686; PMCID: PMC4743316.
9. Marashi SM, Majidi M, Raji Asadabadi H, Nasri-Nasrabadi Z. A common misconception in the management of aluminium phosphide poisoning. Arh Hig Rada Toksikol 2013;64(3):475–6.
10. Bajwa SJ, Bajwa SK, Kaur J, Singh K, Panda A. Management of celphos poisoning with a novel intervention: A ray of hope in the darkest of clouds. Anesth Essays Res 2010 ;4(1):20-4. doi: 10.4103/0259-1162.69301. PMID: 25885082; PMCID: PMC4173337.
11. Agrawal VK, Bansal A, Singh RK, Kumawat BL, Mahajan P. Aluminum phosphide poisoning: Possible role of supportive measures in the absence of specific antidote. Indian journal of critical care medicine: peer-reviewed, official publication of Indian J Crit Care Med 2015 ;19(2):109.
12. Shadnia S, Rahimi M, Pajoumand A, Rasouli MH, Abdollahi M. Successful treatment of acute aluminium phosphide poisoning: Possible benefit of coconut oil. Hum Exp Toxicol 2005;24(4):215–8.
13. Chugh SN, Kumar P, Aggarwal HK, Sharma A, Mahajan SK, Malhotra KC. Efficacy of magnesium sulphate in aluminium phosphide poisoning - comparison of two different dose schedules. J Assoc Physicians India 1994;42(5):373–5.
14. Singh UK, Chakraborty B, Prasad R. Aluminium phosphide poisoning: A growing concern in pediatric population. Indian Pediatr 1997; 34(7):650–1.
15. Siwach SB, Singh P, Ahlawat S, Dua A, Sharma D. Serum and tissue magnesium content in patients of aluminium phosphide poisoning and critical evaluation of high dose magnesium sulphate therapy in reducing mortality. J Assoc Physicians India 1994;42(2):107–10.
16. Sahoo D, Kujur ST, Das DS, Dey A, Devi S. Aluminium Phosphide Poisoning: Early Suspicion of Cardiotoxicity Is Necessary for Improved Outcomes. Cureus 2020;12(9):e10237. doi: 10.7759/cureus.10237. PMID: 33042678; PMCID: PMC7535943.
17. Oghabian Z, Ahmadi J, Pakravan S, Dabaghzadeh F, Heidari MR, Tajaddini S. Successful treatment of aluminium phosphide poisoning by dihydroxyacetone: A two-case report study. J Clin Pharm Ther 2020; 45(5):1194-98. DOI: 10.1111/jcpt.13194. PMID: 32526065.
18. Niknahad H, Heidari R, Hashemi A, Jamshidzadeh A, Rashedinia M. Antidotal effect of dihydroxyacetone against phosphine poisoning in mice. J Biochem Mol Toxicol 2021;27:e22897.
19. Rashedinia M, Jamshidzadeh A, Mehrabadi AR, Niknahad H. Prevention of phosphine-induced cytotoxicity by nutrients in HepG2 cells. Indian J Med Res 2016; 144(4):560-565. doi:10.4103/0971-5916.200896. PMID: 28256464; PMCID: PMC5345302.

***Corresponding Author**
Dr. Harish R
Associate Professor, Department of Biochemistry,
Sri Devaraj Urs Medical College,
Sri Devaraj Urs Academy of Higher Education and Research,
Tamaka, Kolar -563101, Karnataka, India.
Mobile No : 9845955050
E-mail: harishreddy1349@gmail.com